

**REMARKS**

As a preliminary matter, Applicants thank the Examiner for his indication that claims 50 and 52 are allowable. Claims 1 to 33 and 39 to 53 are pending in this application. Claims 39 to 45 have been canceled. Claims 1 to 3, 6, 10 to 17, 21 to 25, 32, 33, and 46 to 53 have been amended. Support for the amendments can be found throughout the specification, for example, at page 2, lines 30 to 31 (pharmaceutically acceptable salts of the compounds of the invention). No new matter has been added. After entry of this amendment, claims 1 to 33 and 46 to 53 will be pending in this application.

**I. Supplemental Information Disclosure Statement**

Applicants have enclosed a supplemental information disclosure statement and hereby authorize the Commissioner to deduct the appropriate fee.

**II. Terminal Disclaimer**

Applicants have enclosed a terminal disclaimer signed by the attorney of record, Paul Legaard, and have authorized the Commissioner to deduct the appropriate fee.

**III. Claim Rejections under 35 U.S.C. § 112, second paragraph**

Claims 1, 12, 47 to 49, 51, and 53 are rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to point out and distinctly claim the subject matter which Applicants regard as their invention. First, the Office alleges that the phrase “optionally substituted” in claims 1 and 12 is indefinite for failing to list the particular substituents in the definitions. As to the term “optionally substituted” in the definitions of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>6</sup>, and R<sup>7</sup>, Applicants respectfully point out that each definition further recites that “all such optional substitutions are made with 0, 1, 2 or 3 R<sup>e</sup> moieties” and that R<sup>e</sup> is clearly defined.

As to the term “optionally substituted” for R<sup>4</sup>, claims are indefinite when, read in light of the specification, they do not reasonably apprise those skilled in the art of the scope of the invention. *Howmedia Osteonics v. Tranquil Prospects*, 401 F.3d 1367, 1371 (Fed. Cir. 2005). However, the claims must be so insolubly ambiguous that no narrowing construction can

properly be adopted. When a claim “is not insolubly ambiguous, it is not invalid for indefiniteness.” *Bancorp v. Hartford Life*, 359 F.3d 1367, 1372 (Fed. Cir. 2004). Claims need not be plain on their face in order to avoid condemnation for indefiniteness; rather, what the examiner is asked is whether the claims are amenable to construction. *SmithKline v. Apotex*, 403 F.3d 1331, 1340 (Fed. Cir. 2005), citing *Exxon Research & Engineering Corp. v. United States*, 265 F.3d 1371, 1375 (Fed. Cir. 2001).

Given the standards described above, neither the term “optionally” nor the term “substituted” is unusual. In particular, Applicants’ specification clearly defines what is meant by “optionally substituted” with many examples of the substituents (see specification at page 31, lines 7 to 18 ). In light of the definition of “optionally substituted” and the clarifying phrase in the definitions of R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>6</sup>, and R<sup>7</sup>, Applicants respectfully assert that the amended claims meet the requirements of 35 U.S.C. § 112, second paragraph, and request that the claim rejections be withdrawn.

Second, the Office alleges that the phrase “*in vivo* hydrolysable ester” in claim 47 is indefinite. While maintaining that one of ordinary skill would understand what is meant by this term, Applicants have deleted this phrase from claim 47, rendering the rejection moot. Applicants respectfully assert that the amended claim meets the requirements of 35 U.S.C. § 112, second paragraph, and request that the claim rejections be withdrawn.

Third, the Office alleges that the formulas in claims 48, 49, and 53 have dangling valencies for some of the nitrogen atoms. Applicants respectfully assert that chemical formulas are well understood to contain hydrogen atoms, even when not drawn, where necessary to maintain the proper valency of the atom in the formula. However, solely to advance prosecution, Applicants have amended claims 48, 49, and 53, as well as claims 1, 12, 23, and 51. Applicants respectfully assert that the amended claims meet the requirements of 35 U.S.C. § 112, second paragraph, and request that the claim rejections be withdrawn.

#### **IV. Claim Rejections under 35 U.S.C. § 112, first paragraph**

Claims 39 to 46 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the enablement requirement. While maintaining that undue experimentation

would not be required to use the claimed invention, Applicants have canceled claims 39 to 45, reciting methods of preventing various disorders, solely to advance prosecution.

Further, the Office has rejected claims 27 and 28, alleging that there is no way to predict what neurological disorder is associated with  $\beta$ -amyloid production. As claims 27 and 28 are compound claims which do not recite the term “neurological disorders associated with  $\beta$ -amyloid production”, Applicants assume that the rejection is drawn to claim 39 which does recite this term. While believing that one of ordinary skill could determine what neurological disorders are associated with  $\beta$ -amyloid production, Applicants have canceled claim 39, solely to advance prosecution.

After cancellation of claims 39 and 43 to 45, the pending claims are drawn to methods of inhibiting  $\gamma$ -secretase activity (claim 46). Applicants respectfully assert that the remaining claim can be practiced without undue experimentation.

As will be recognized, the enablement requirement of § 112 is satisfied so long as a disclosure contains sufficient information that persons of ordinary skill in the art having the disclosure before them would be able to make and use the invention. *In re Wands*, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988) (the legal standard for enablement under §112 is whether one skilled in the art would be able to practice the invention without undue experimentation). In this respect, the following statement from *In re Marzocchi*, is noteworthy:

As a matter of Patent Office practice, then, a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented **must** be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt does exist, a rejection for failure to teach how to make and/or use will be proper on that basis; such a rejection can be overcome by suitable proofs indicating that the teaching contained in the specification is truly enabling.

... it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of

any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

169 U.S.P.Q. 367, 369-370 (C.C.P.A. 1971) (emphasis added). Thus, any assertion by the Patent Office that an enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed. *In re Dinh-Nguyen*, 181 U.S.P.Q. 46 (C.C.P.A. 1974); *In re Bowen*, 181 U.S.P.Q. 48 (C.C.P.A. 1974).

In contravention of its burden under *In re Marzocchi*, the Office has failed to provide any evidence or reasoning why undue experimentation would be required to use the method of inhibiting  $\gamma$ -secretase activity as recited by claim 46. Applicants' specification teaches that the compounds of the invention have been shown to inhibit  $\beta$ -amyloid production, as determined by a  $\gamma$ -secretase detergent assay and  $\gamma$ -secretase whole cell assay (page 89, line 23, through page 92, line 2). Given the teachings of the specification, one of ordinary skill be able to use the claimed method without undue experimentation. Accordingly, Applicants respectfully assert that claim 46 is enabled and request that the claim rejection be withdrawn.

## **V. Obviousness-type Double Patenting**

Claims 23-33 are provisionally rejected over claims 1 to 9 and 12 to 23 of U.S. Patent Appl. No. 10/528,640 on the basis of nonstatutory obviousness-type double patenting. As a terminal disclaimer is included with this response, Applicants respectfully request that the claim rejections based on obviousness-type doubling patenting be withdrawn.

## **VI. Conclusion**

Applicants respectfully request reconsideration of the rejections of record in light of the comments and amendments above. Further, early reconsideration and allowance of all pending claims is respectfully requested.

The Commissioner is hereby authorized to debit any fee due or credit any overpayment to deposit account 50-0436.

Respectfully submitted,

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Enclosures: Terminal Disclaimer  
Supplemental Information Disclosure Statement